

Verrucous carcinoma: A clinicopathological study

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Abstract

Objective: The purpose of this study is to identify a co-relation between clinical and histopathological features of verrucous carcinoma.

Materials and Methods: This study was conducted based on Knowledge Attitude and Practice (KAP) questionnaire comprising of 3 sets of questions covering clinical and histopathological aspects of the oral verrucous carcinoma. The target subjects were specialists in the field of Oral Medicine and Radiology, Oral and Maxillofacial Surgery and Oral Pathology.

Results and Conclusion: Verrucous carcinoma is a low grade variant of squamous cell carcinoma and the clinical features of both are very similar. The treatment of both differs widely; we fail to diagnose it correctly. This study correlates the clinic-pathologic features of oral verrucous carcinoma by means of statistically analyzing the varied clinical features and pathological impressions. This is helpful in eliminating the diagnostic dilemma and thus channelizing the data to present a clear treatment planning.

Keywords: Oral verrucous carcinoma, oral verrucous hyperplasia, oral verrucous keratosis

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INTRODUCTION

Ackerman first described the oral verrucous carcinoma (OVC).^[1] It is a well-differentiated form or low-grade variant of squamous cell carcinoma with varied clinical and histological features. In many literatures, various synonyms have been attributed to describe this entity including Ackerman's tumor, florid oral papillomatosis, Buschke–Lowenstein tumor, epithelioma cuniculatum and carcinoma cuniculatum.^[2] OVC is a rare tumor represent which only 3%–4% of all oral carcinomas. The etiopathogenesis of OVC is not very clear, although there is a strong association has been noted with the use of tobacco, poor oral hygiene and alcohol. The tumor growth is slow, and

it has a locally invasive nature but unlikely to metastasize. It usually appears as a painless, thick white plaque resembling a cauliflower. The most common sites of oral mucosal involvement include the buccal mucosa, followed by the mandibular alveolar crest, gingiva and tongue. A condition known as verrucous hyperplasia was described by Shear and Pindborg^[3] in 1980 which has been considered as an antecedent or early stage of verrucous carcinoma (VC). Both of these lesions closely resemble each other clinically as well as pathologically.^[4,5] Surgery with wide margins is considered the primary mode of treatment.^[6] However, surgery combined with radiotherapy is the next most preferable treatment and may have benefits, particularly in cases of

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extensive lesions.^[7] The recurrence rate is high in cases in which either irradiation or surgery alone is performed.

The purpose of this article is to correlate the clinical and the histopathological features of the VC based on the perception of various specialists in the field of oral medicine and radiology, oral and maxillofacial surgery and oral pathology.

MATERIALS AND METHODS

A thorough literature search was performed to understand and identify the updates in the field of OVC. Electronic database PubMed was searched from 2012 up to 2017 for the relevant literature using key phrase of “OVC” and reference articles of the selected article were referred. We included systematic reviews and case reports. Only articles reported in English were considered for review and a knowledge, attitude and practice (KAP) questionnaire was designed based on the literature from these articles.

This is a questionnaire-based cross-sectional survey study comprising 32 monocentric respondents. These respondents were postgraduates and staff members of

various specialties of oral medicine and radiology, oral and maxillofacial surgery and oral pathology from same.

This was a “KAP” questionnaire (KAP) [Figures 1 and 2].

“Knowledge” respondents were evaluated by five closed-ended questions having two options each (Yes/No). It was evaluated by arithmetic percentage.

“Attitude” of the respondents was evaluated based on a 4-point Likert scale (Agree/Disagree/Strongly Agree/Strongly Disagree), which was evaluated by *t*-test.

“Practice” was evaluated as similar to knowledge by plain arithmetic percentage.

RESULTS

All 32 respondents responded positively to the questionnaire. On the evaluation of knowledge and practice, there was an overwhelming correct response of 93% by the respondents for the knowledge-based questions on “characteristic clinical features with gender predominance” and 88.75% for the practice-based questions on “prevalence and site of OVC, incidence of bleeding and treatment option” while the number of wrong responses was a staggering 7% and 11%, respectively [Table 1].

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This is a knowledge, attitude and practice based questionnaire to assess the perception of specialists in the field of Oral Medicine, Oral Pathology and Oral Surgery towards the clinical presentation, histopathological features and treatment towards Oral Verrucous Carcinoma.

The respondents need not reveal their identity.

Speciality- _____ Code No.- _____

Title of the study- Clinicopathologic Study of Verrucous Carcinoma by using the KAP Questionnaire.

Q1. Is verrucous carcinoma characterized by exophytic growth?
YES NO

Q2. Does verrucous carcinoma occur more in males than females?
YES NO

Q3. Is the growth seen in verrucous carcinoma painless?
YES NO

Q4. Is parakeratin plugging a histopathological feature in verrucous carcinoma?
YES NO

Q5. Are the papillary projections evident on histopathological examination of verrucous carcinoma?
YES NO

Q6. Verrucous carcinoma is generally seen in elderly patients with the mean age of occurrence being 60-70 years.
AGREE/ STRONGLY AGREE/ DISAGREE/ STRONGLY DISAGREE

Q7. Regional lymphadenopathy is often seen in verrucous carcinoma.
AGREE/ STRONGLY AGREE/ DISAGREE/ STRONGLY DISAGREE

Figure 1: Knowledge, attitude and practice questionnaire

Q8. In verrucous carcinoma, tenderness and induration are evident on palpation.
AGREE / STRONGLY AGREE / DISAGREE / STRONGLY DISAGREE

Q9. Histopathologic examination of verrucous carcinoma shows broad pushing rete-pegs without invasion.
AGREE/ STRONGLY AGREE/ DISAGREE/ STRONGLY DISAGREE

Q10. Minimal cellular atypia is evident on histopathologic examination of verrucous carcinoma.
AGREE/ STRONGLY AGREE/ DISAGREE/ STRONGLY DISAGREE

Q11. Is incidence of bleeding seen rarely in verrucous carcinoma?
YES NO

Q12. Is verrucous carcinoma seen in decreasing order of the following common intraoral sites?
Buccal mucosa> Mandibular alveolar crest> Gingival> Tongue.
YES NO

Q13. Is the prevalence of verrucous carcinoma high in tobacco chewers?
YES NO

Q14. Should the treatment of verrucous carcinoma be entirely surgical?
YES NO

Q15. Is the prognosis of verrucous carcinoma better than usual type of oral epidermoid carcinoma?
YES NO

Figure 2: Knowledge, attitude and practice questionnaire

The objective of evaluating “attitude” in this study was to draw out the intensity of response by the respondents toward various clinical and histopathologic aspects of OVC which can lead to a correct diagnosis. A *t*-test was done for the 4-point Likert scale at a confidence interval of 95% for which $P < 0.005$ which was statistically significant. Responses of the respondents were proportionate in respect to the questions attributing to “mean age of occurrence, tenderness and induration, regional lymphadenopathy and evidence on histopathologic examination of OVC” [Figure 3].

However, the respondents gave a relatively contrasting opinion on the aspect of tenderness and induration on palpation in OVC [Table 2].

T-test analysis was done to find a correlation between questions pertaining to attitude. Parameters (Agree/Disagree/Strongly agree/Strongly disagree) were compared with statistically significant ($P < 0.005$) [Table 3].

DISCUSSION

Schrader *et al.*^[8] and Jordan^[9] described VC s as slow-growing, well-demarcated, exophytic and hyperkeratotic lesions. The etiology of VC is not well defined.^[10] VC (VC) is a nonmetastasizing variant of well-differentiated squamous cell carcinoma (SCC), which often presents as an exophytic, warty tumor. The oral cavity is the most common site in which the buccal mucosa, tongue, alveolar ridge and lips are the areas usually involved. It typically occurs in elderly patients with predilection for males in fourth to sixth decade which may become locally invasive if not treated properly.^[11] Metastasis to regional lymph node is very rare, and distant metastases have not been reported. Palpable enlarged lymph nodes are often reactive. Leukoplakias or erythroplakias, as well as proliferative verrucous leukoplakia, are the previous lesions where the OVC used to arise from.^[11] Its etiology is not well-known, but smoking habit,

alcohol consumption and betel nut chewing are proved causes.^[12] According to the recent theories, types of human papillomavirus cause the nullification of tumor suppressor gene concerning the pathogenesis of the VC. Although the oncogenic role of HPV in OVC is not of much importance as that of the SCC oncogenesis.^[13] Chronic repetitive mechanical traumas/irritation may contribute to VC.^[14,15] The classical histopathological features include intact basement membrane, without disruption of stratification and broad rete pegs, which appear to punch into the underlying tissue. The most important pathological difference between VC and squamous cell carcinoma is that there is a good cytological differentiation throughout the tumor in case of VC.^[16] Histopathologically, VC can also be mistakenly diagnosed as a benign lesion. Head and neck VC is highly associated with smoking. The presence of potentially malignant lesions such as oral lichen planus, leukoplakia, erythroplakia and poor oral hygiene may also act as predisposing factors.^[17]

In a study done by Ackerman, out of 18 patients, 11 patients (61%) with buccal cancers were tobacco chewers.^[18] Shear and Pindborg^[3] reported that out of

Table 1: Data representing the percentage of affirmative and negative responses of knowledge and practice of knowledge, attitude and practice questionnaire

Question	n	Affirmative responses (%)	Negative responses (%)
1		96.8	3.2
2		90.6	9.4
3		87.5	12.5
4		93.7	6.3
5		96.9	3.1
11		75	25
12		96.9	3.1
13		87.5	12.5
14		87.5	12.5
15		96.9	3.1

Table 2: Data representing the percentage of responses of the attitude of knowledge, attitude and practice questionnaire

Question	n	Responses (%)			
		Agree	Strongly agree	Disagree	Strongly disagree
6		62.5	34.3	9.3	0
7		59.3	12.5	21.9	6.3
8		53	6.3	34.4	6.3
9		59.4	28.1	12.5	0
10		65.6	15.6	15.6	3.2

Table 3: “T”-test for dependent mean at $P < 0.05$ as statistically significant

Parameter	n	Total (n)	t	P
Strongly agree	31	160	-2.49	0.0335
Strongly disagree	5	160		
Agree	96	160	-6.65	0.0013
Disagree	30	160		

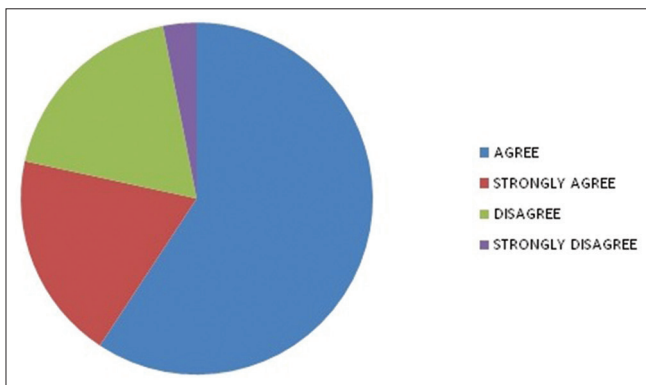


Figure 3: Responses for attitude-based questions

28 patients with verrucous lesions, 24 (86%) used tobacco and one was an areca quid chewer. Tobacco appears to be a major factor in the causation of verrucous lesions.^[19] In Chen *et al.*'s^[17] study of VCs in Taiwan, areca quid chewing has been reported by 97.3%.^[20]

Verrucous hyperplasia is a forerunner of VC, and transition is so consistent that the hyperplasia, once diagnosed, should be treated as VC. Therefore, verrucous hyperplasia should clinically be closely followed up to intercept and prevent such a possibility.

The differential diagnosis can be made on basis histological diagnosis. Verrucous hyperplasia does not extend into deeper tissues generally and is superficial in nature, whereas VC extends more deeply.^[21]

Alcohol consumption alone or in conjunction with tobacco usage also have shown an increased risk of carcinogenesis.^[22]

In the current literature,^[23] although the most commonly involved site for VC is the buccal mucosa, the most affected areas in the present studies were the mandibular retromolar and molar area (41.6%) followed by the buccal mucosa (16.6%), the hard palate (16.6%), the floor of the mouth (16.6%) and the lip mucosa (8.3%).

Regional lymph nodes are often tender and enlarged in case of OVC because of inflammatory involvement, which may simulate the metastatic tumor.^[24]

Histologically, VC typically has a heavily parakeratinized epithelium or irregular clefted surface with parakeratin plugging extending deeply into the clefts. The tumor has a well-defined basement membrane without any disruption in continuity with bulbous hyperplasia seen in the prickle cell layers. There is minimal atypia, and usually, there is the presence of subepithelial inflammatory.^[25]

The prognosis of VC is better than that of other kinds of life-threatening malignant tumors. Surgery is the most commonly considered treatment option for VC.

Irradiation alone or in combination with surgery is rarely performed. The combination therapy can be administered in case of tumor extending to retromolar area.^[6,26] McClure *et al.* reported that extensive lesions in the oral cavity may benefit from combined therapy. Other treatment modalities such as cytostatic drugs may be preferred when surgery is not indicated.^[7]

CONCLUSION

There is a very subtle line between the features of OVC and oral squamous cell carcinoma. Hence, the probability of the misdiagnosis of the OVC is more. This research article helps in channelizing the clinical and histopathological findings into a concrete diagnosis and appropriate treatment planning by the help of observations and experiences of oral and maxillofacial specialists. The knowledge and clinical aptitude of dental professionals were well highlighted by our KAP questionnaire which was analyzed. This, in turn, concluded the perception of the dentists regarding the most common clinical features of OVC and its correlation with the histopathological features.

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Conflicts of interest

There are no conflicts of interest.

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